

## ARTIFACT SHEET

Enter artifact number below. Artifact number is application number + artifact type code (see list below) + sequential letter (A, B, C ...). The first artifact folder for an artifact type receives the letter A, the second B, etc..

Examples: 59123456PA, 59123456PB, 59123456ZA, 59123456ZB

08157564 BA  
Indicate quantity of a single type of artifact received but not scanned. Create individual artifact folder/box and artifact number for each Artifact Type.

☐

CD(s) containing:

computer program listing

Doc Code: Computer

pages of specification

and/or sequence listing

and/or table

Doc Code: Artifact

content unspecified or combined

Doc Code: Artifact

☐

Artifact Type Code: P

☐

Artifact Type Code: S

☐

Artifact Type Code: U

☐

Stapled Set(s) Color Documents or B/W Photographs

Doc Code: Artifact    Artifact Type Code: C

☐

Microfilm(s)

Doc Code: Artifact    Artifact Type Code: F

☐

Video tape(s)

Doc Code: Artifact    Artifact Type Code: V

☐

Model(s)

Doc Code: Artifact    Artifact Type Code: M

☒

Bound Document(s)

Doc Code: Artifact    Artifact Type Code: B

☐

Confidential Information Disclosure Statement or Other Documents marked Proprietary, Trade Secrets, Subject to Protective Order, Material Submitted under MPEP 724.02, etc.

Doc Code: Artifact    Artifact Type Code X

☐

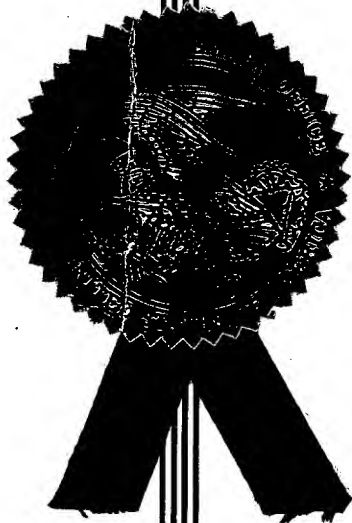
Other, description: \_\_\_\_\_

Doc Code: Artifact    Artifact Type Code: Z

A-677

U.S. Pat. No. 4,816,484

# The United States of America



## The Commissioner of Patents and Trademarks

*Has received an application for a patent  
for a new and useful invention. The title  
and description of the invention are en-  
closed. The requirements of law have  
been complied with, and it has been de-  
termined that a patent on the invention  
shall be granted under the law.*

*Therefore, this*

## United States Patent

*Grants to the person or persons having  
title to this patent the right to exclude  
others from making, using or selling the  
invention throughout the United States  
of America for the term of seventeen  
years from the date of this patent, sub-  
ject to the payment of maintenance fees  
as provided by law.*

Commissioner of Patents and Trademarks

*Melvinia Gary*  
Attest

## NOTICE

*If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number, and timing of the maintenance fees required may be changed by law or regulation.*

**United States Patent** [19]  
**Toyoshima et al.**

[11] **Patent Number:** 4,816,484  
[45] **Date of Patent:** Mar. 28, 1989

[54] **HYPOGLYCEMIC AGENT**

[75] **Inventors:** Shigeshi Toyoshima; Yoshiko Seto,  
both of Funabashi; Hisashi Shinkai,  
Kawasaki; Koji Toi, Kanagawa;  
Izumi Kumashiro, Yokohama, all of  
Japan

[73] **Assignee:** Ajinomoto Co., Inc., Tokyo, Japan

[21] **Appl. No.:** 146,719

[22] **Filed:** Jan. 21, 1988

**Related U.S. Application Data**

[62] Division of Ser. No. 844,970, Mar. 27, 1986, abandoned.

[30] **Foreign Application Priority Data**

Mar. 27, 1985 [JP] Japan ..... 60-62276

[51] **Int. Cl.<sup>4</sup>** ..... A61K 31/215; C07C 101/72

[52] **U.S. Cl.** ..... 514/563; 514/529;  
514/530; 549/304; 549/467; 562/445; 562/450;  
560/40; 560/41; 546/169; 546/323

[58] **Field of Search** ..... 514/563, 613; 562/445;  
560/40

[56] **References Cited**

**U.S. PATENT DOCUMENTS**

4,670,584 6/1987 Toyoshima et al. .... 562/445

**FOREIGN PATENT DOCUMENTS**

93551 9/1983 European Pat. Off. .  
2102412 2/1983 United Kingdom .

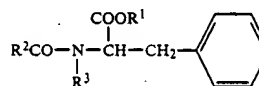
**OTHER PUBLICATIONS**

Toyoshima et al., "Preparation of D-Phenylalanine  
Derivatives and Their Use as Hypoglycemic Agents",  
CA 106 85057d (1987).  
European Search Report/Application No. 86 30  
2217/26-11-1987.

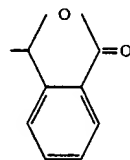
*Primary Examiner*—Glennon H. Hollrah  
*Assistant Examiner*—A. A. Owens  
*Attorney, Agent, or Firm*—Oblon, Fisher, Spivak,  
McClelland & Maier

[57] **ABSTRACT**

A compound of D-phenylalanine derivative for hypo-  
glycemic use, represented by the general formula



$R^1$  is selected from hydrogen, alkyl of 1 to 5 carbon  
atoms, aryl of 6 to 12 carbon atoms, aralkyl of 6 to 12  
carbon atoms,



$-CH_2CO_2R^3$ ,  $-CH(CH_3)-OCO-R^3$ , and  $-CH_2-OCO-C(CH_3)_3$ ;  $R^2$  is selected from groups comprising aryl of 6 to 12 carbon atoms, a hetero six-membered ring, a hetero five-membered ring, cycloalkyl, or cycloalkenyl, any of which groups may have one or more substituents; and  $R^3$  is selected from hydrogen and alkyl of 1 to 5 carbon atoms; the salts thereof, and precursors which can be converted thereto in the human or animal body.

Some of the compounds are novel per se.

**15 Claims, No Drawings**